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March 25, 2003

PLEASE DELIVER AS SOON AS POSSIBLE TO:

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1. Examiner T. Saida - Group Art Unit 1642	United States Patent & Trademark Office	703-746-3156	

Total number of pages including this page: 6

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Re: Fastrez, et al.
Serial No. 08/978,607
Filed: November 26, 1997
Chimeric Target Molecules Having a Regulatable Activity
Our File No. 100390-09650

PATENTS
100390-09650

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Pastrez et al.
Serial No. : 08/978,607
Filed : November 26, 1997
For : **CHIMERIC TARGET MOLECULES HAVING A
REGULATABLE ACTIVITY**
Group Art Unit : 1642
Examiner : T. Saidha

I hereby certify that this correspondence is
being faxed to 703-746-3156 to Examiner
T. Saidha of the United States Patent and
Trademark Office in Washington, D.C. 20231
on March 25, 2003

Gerard Bilotta, Reg. No. 51,474

Name of Applicant, Assignee


Signature

March 25, 2003

Date of Signature

Assistant Commissioner for Patents
Washington, D.C. 20231

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Applicants respectfully submit this Supplemental Information Disclosure Statement pursuant to 37 C.F.R. §§ 1.97, 1.98 and 37 C.F.R. § 1.56. These references are listed herein and on Form PTO/SB/08 submitted herewith. It is respectfully requested that the information be expressly considered during the prosecution of this application and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom. The Examiner's attention is also directed to the following documents. A copy

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of each of the documents was submitted under separate cover via FedEx (No. 824356335220) on March 24, 2003. Form PTO/SB/08, is enclosed herewith and submitted in duplicate.

The Examiner's attention is hereby called to the fact that this application is a Continuation-in-Part of Serial No. 08/757,425 filed November 27, 1996.

1. Brennan C et al., (1994), "Modulation of enzyme activity by antibody binding to an alkaline phosphatase - epitope hybrid protein", *Protein Engineering*, 7(4): 509-514.
2. Brennan C et al., (1995), "A Modular sensor system based on genetically engineered alkaline phosphatase", *Proc Natl Acad Sci*, 92: 5783-5787.
3. Benito A et al., (1996), " β -Galactosidases Enzymatic Activity as a Molecular Probe to Detect Specific Antibodies", *J Biol Chem*, 271(35): 21251-21256.
4. Feliu JX et al., (1998), "Distinct Mechanisms of antibody-mediated enzymatic reactivation in β -Galactosidases molecular sensors", *FEBS Letts*, 438: 267-271.
5. Ferrer-Miralles et al., (2001), "Engineering Regulable Escherichia coli β -Galactosidases as Biosensors for Anti-HIV Antibody Detection in Human Sera" *J. Biol. Chem.* 276 (43):40087-40095.
6. Lu Z et al., (1995), "Expression of Thioredoxin Random Peptide Libraries on the Escherichia coli Cell Surface as Functional Fusions to Flagellin: A System Designed for Exploring Protein-Protein Interactions", *Biotechnol*, 13: 366-372.
7. Norman TC et al., (1999), "Genetic Selection of Peptide Inhibitors of Biological Pathways", *Science*, 285: 591-595.
8. Legendre D et al., (1999), "Engineering a regulatable enzyme for homogeneous immunoassays", *Nature Biotechnol*, 17: 67-72.

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9. Legendre D et al., (2002), "TEM-1 β -lactamase as a Scaffold for protein recognition and assay", *Protein Sci*, 11: 1506-1518.

10. Skerra A, (2000), "Engineering protein scaffolds for molecular recognition", *J Mol Recognition*, 13: 167-187.

This Information Disclosure Statement is not a representation that the documents cited herein are considered most pertinent, or that a search has been undertaken, or that any of the cited documents is indeed prior art. The Examiner is invited to undertake an independent search.

No fee is believed necessary for entry and consideration of this Information Disclosure Statement. However, the Commissioner is hereby authorized to charge any fee required or credit any overpayment in such fees to Deposit Account No. 50-0540.

Applicants respectfully request that a copy of PTO/SB/08, appropriately initialed by the Examiner, be returned to Applicants' attorney.

Respectfully submitted,

KRAMER LEVIN NAFTALIS & FRANKEL LLP
Attorneys for Applicants

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March 24, 2003

VIA FEDERAL EXPRESS

Examiner T. Saida
Crystal Mall One - Room 10D03
1931 Clark Street
Arlington, VA 22202

Group Art Unit 1642

Re: U.S. Patent Application Ser. No. 08/978,607
Title: *Chimeric Target Molecules Having a
Regulatable Activity*
Igen International, Inc.
Our File No.: 100390-09650

Dear Examiner Saida:

Applicants would like to thank the Examiner for the telephonic interview on March 20, 2003. As per our discussion we are submitting the following ten articles for the Examiner's convenience.

1. Brennan C et al., (1994), *Protein Engineering*, 7(4): 509-514. ✓
2. Brennan C et al., (1995), *Proc Natl Acad Sci*, 92: 5783-5787. —
3. Benito A et al., (1996), *J Biol Chem*, 271(35): 21251-21256. ✓
4. Feliu JX et al., (1998) *FEBS Letts*, 438: 267-271. —
5. Ferrer-Miralles et al., (2001), *J. Biol. Chem.* 276 (43):40087-40095. —
6. Lu Z et al., (1995), *Biotechnol*, 13: 366-372. —
7. Norman TC et al., (1999), *Science*, 285: 591-595. —
8. Legendre D et al., (1999), *Nature Biotechnol*, 17: 67-72. ✓

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9. Legendre D et al., (2002), *Protein Sci*, 11: 1506-1518.

10. Skerra A, (2000), *J Mol Recognition*, 13: 167-187.

Articles 1 and 2 by Brennan and co-workers describe the modulation of the enzymatic activity of alkaline phosphatase by inserting an epitope into a sequence of the enzyme.

The authors of Articles 3, 4 and 5 describe the insertion of binding site moieties into the sequence of galactosidase to modulate the enzymatic activity.

Article 6 shows that random peptide libraries were inserted into native thioredoxin and displayed on the bacterial cell surface. The authors demonstrate a mimotope insertion into the sequence of an enzyme. The construct used by these authors does not involve the methods of the present invention.

Norman et al. in article 7 describes pentapeptides displayed on the surface of inactivated staphylococcal nuclease and Legendre et al. in articles 8 and 9 described the follow-up engineering of β -lactamase, as described in the instant application.

The selected references describe the engineering of five distinct enzymes. Therefore, Applicants urge that one of skill in the art would be able to practice the presently claimed subject matter in view of the specification and the high state of the relevant art without undue experimentation.

Finally, the review article 10 by Skerra is representative of the high state of relevant art.

After reviewing these articles please call the undersigned attorney to discuss any further questions that you may have before the issuance of an Office Action.

Sincerely,



Gerard Bilotto, Esq.
Reg. No. 51,474

GB:dmp
Enclosures

cc: Barry Evans, Esq. (w/o enclosures)
Reg. No. 22,802